## REMARKS

Claims 1-4 and 6-12 stand finally rejected under 35 U.S.C. § 103(a) as being unpatentable Chopdekar et al.(US 5,663,415 hereinafter referred to as the '415 patent), Gordziel (US 6,287,597, referred to as the '597 patent) and Sikora et al. (US 6,268,012, hereinafter referred to as the '012 patent). This rejection is respectfully traversed in view of the amendment to claim 1, the remarks set forth below and the accompanying Declaration Under 35 C.F.R. § 1.132. It is conceded that the '415 patent is pertinent and most of the remarks set forth below will be directed to the patentable distinctions between the invention as set forth in the claims as amended.

In order to narrow the issues, it is **conceded** that it is well known to dehydrate pharmaceutical compounds by using a dying medium containing nitrogen, as taught in the '012 patent. It is also **conceded** that drying a pharmaceutical composition under vacuum at moderate temperatures is also old in the art. It is further **conceded** that milling a pharmaceutical composition to a particular particle size is old in the art. Therefore, claims 6-9 are concededly not in and of themselves patentable over the prior art. However, claims 6-9 are **dependent** claims and derive their patentability from **independent claim 1 as amended**. Therefore, it follows that if claim 1 is deemed patentable over the prior art, the dependent claims which contain further limitations should also be patentable.

The '597 patent is not pertinent since the disclosure therein refers to carrying out the reaction between diphenhydramine and tannic acid and a volatile solvent such as isopropanol (see col. 1, line 60 to column 2, line 6). In contradistinction to the isopropanol route, the present invention entails the reaction between diphenhydramine free base and tannic acid under **hot melt** conditions. The examiner's attention is respectfully drawn to page 2, lines 21-26, of the instant specification which discloses the disadvantages of the isopropanol route:

> Commercially available antihistamine tannate compositions are relatively impure. Such compositions are typically prepared by reacting the antihistamine free base with tannic acid in the presence of a volatile solvent, usually isopropanol. The yield is only fair (e.g. about 70%) and the decomposition products, e.g., 2-5 wt%, and a significant amount of the volatile solvent, e.g., 6-10 wt.%, based on the weight of the composition, remains with the product and cannot be removed.

How then to prepare diphenhydramine tannate in a manner that would produce a pure pharmaceutical composition free of impurities and any volatile solvents? The invention disclosed and claimed in the '415 patent solves this dilemma by carrying out the reaction between the diphenhydramine free base and the tannic acid in the presence of 50 wt.% water at a moderate reaction temperature, i.e. 65-70°C. However, the problem is then posed as to how to recover the diphenhydramine tannate product from the reaction mixture. The '415 patent discloses that this latter problem was solved by subjecting the aqueous reaction mixture to freeze drying at a pressure of not greater than about 500 milliTorre and a temperature of about -60 to about -20°C. Note that as brought out in the enclosed Rule 132 Declaration, **it is not feasible to recover the diphenhydramine tannate by subjecting the aqueous reaction mixture to conventional vacuum oven treatment.**

The question is then presented as to how to prepare pure diphenhydramine tannate containing no extraneous volatile solvents and at the same time, avoiding the use of expensive, time-consuming freeze-drying processes. This problem has been solved by the instant invention in which diphenhydramine free base is reacted with tannic acid by a **hot melt** process, i.e., a process in which there is a maximum of 20 wt.% water present (to facilitate stirring during the reaction) and the reaction is carried out at elevated temperatures, i.e., temperatures of 75 to 150°C. It is respectfully submitted that the hot melt process of the instant invention is clearly patentable over the process set forth in the '415 patent for the reasons set forth below.

The attention of the Examiner is respectfully drawn to the reasons for allowance of two other related patent applications examined by the **same** Examiner. For the convenience of the Examiner, the following portions of the reasons for allowance have been duplicated below:

S.N. 10/326,349 filed 12/20/2002, allowed 7/23/2004 (patent not yet issued) claims a hot-melt process for preparing carbinoxamine tannate, and the principal cited reference was Chopdekar et al. (US 5,663,415). In his Reasons for Allowance attached to the Notice of Allowability mailed 7/15/2004, Examiner Oh stated on pages 3-4 that:

- - The instant invention, however, differs from the prior art in that none of the prior art have suggested that the reaction takes place on a hot melt basis under a neat condition which describes that no additional diluent or water, such as water is employed during the process; the specific claimed reaction between the carbinoxamine free base and the tannic acid is carried out at a temperature of 50 to 150°C in the presence of 5 to 30 wt.% water; the claimed drying process is conducted by sparging with nitrogen for a period of 1 to 10 hours or more under vacuum and the claimed particle size is specified.

Furthermore, there is no motivation in the prior art to modify the temperature and water concentration in the claims. In addition, unless all limitations of the claim are met, there is no prior art rejection. See In re Zurko, 59 USPO 2d 1690 (Fed. Cir. 1991) and In re Lee, 61 USPQ 2d 1430 (Fed. Cir. 1991).

Therefore, the claimed invention would not have been obvious to the person with an ordinary skill in the art. - -

In a similar vein, S.N. 10/326,361 filed December 20, 2002 (now US Patent 6,833,360 issued December 21, 2004) claimed a process for preparing pseudoephedrine tannate by reacting pseudoephedrine free base with tannic acid neat or in the additional presence of up to about 30 wt.% water at a temperature of about 80 to about 115°C, and thereafter recovering the resultant pseudoephedrine tannate. In this patent application which was also examined by Examiner Oh, the principal cited reference was again Chopdekar et al. (US 5,663,415). In page 3 of the Reasons for Allowance attached to the Notice of Allowability mailed 4/15/2004, Examiner Oh stated:

- - The instant invention, however, differs from the prior art reference in that the recovered pseudoephedrine tannate is milled to provide the free-flowing powder having the specific particle size; the claimed reaction is carried out at a temperature from 80 to 115°C in the presence of little water or 30 wt.% water. Further, there is no motivation in the prior art to modify the temperature and the concentration of water in the prior art to the claimed temperature range and water concentration at the same time. In addition, unless all limitations of the claim are met, there is no prior art rejection. See In re Zurko, 59 USPO 2d 1690 (Fed. Cir. 1991) and In re Lee, 61 USPQ 2d 1430 (Fed. Cir. 1991).- -

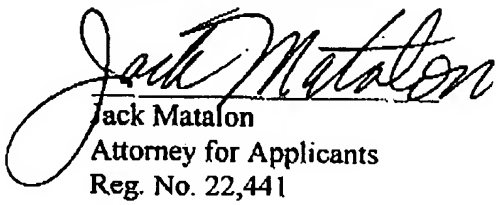
Applicants' attorney respectfully submits that the rationale applied by Examiner Oh in allowing related patent applications S.N. 10/326,349 filed 12/20/2002 and S.N. 10/326,361 filed December 20, 2002 fully applies to claim 1 as amended and claims 2-4 and 6-12 dependent thereon. **The issues involved in the final rejection of claims 1 and 2-4 and 6-12 of the instant application are identical to those presented in the two applications previously allowed by Examiner Oh.** Therefore, the claims in the instant application should be allowed for the same rationale applied by Examiner Oh in allowing S.N. 10/326,349 filed 12/20/2002 and S.N. 10/326,361 filed December 20, 2002.

Further evidence of the non-obviousness of the present invention over the disclosure in the '415 patent is contained in the accompanying Rule 132 Declaration. As noted in the Declaration, it was **not** feasible to recover diphenhydramine tannate from an aqueous reaction mixture containing 50 wt.% water by use of a vacuum oven heated to moderate temperatures. Furthermore, the enclosed Declaration points out the dramatic difference in drying time and processing cost between 30 kg batches of diphenhydramine tannate prepared by the hot melt process of the instant invention versus that prepared by the freeze dry process employed in the '415 patent. The drying time for such batch prepared by the hot melt process of the instant invention was **one-thirteenth** of that prepared by the freeze-dry process employed in the '415 patent while the total processing cost for such batch prepared by the hot melt process of the present invention was **one-eighth** of that prepared by the freeze-dry process employed in the '415 patent. Such results clearly support the premise that the hot melt process of the instant invention is unobvious over the freeze-dry process employed in the '415 patent. Accordingly, the final rejection of claims 1, 2-4 and 6-12 should be lifted and this application should be promptly allowed.

Applicant's attorney respectfully requests the Examiner to re-examine the finally-rejected claims in light of the amendments and remarks set forth above in conjunction with the enclosed Rule 132 Declaration. If the Examiner is so inclined, Applicants' attorney would welcome a telephone interview with the Examiner to discuss what further steps need to be undertaken to advance the prosecution of this application to allowance.

If the Examiner is disposed to maintain his final rejection of claims 1, 2-4 and 6-12, it is respectfully requested that this Response nevertheless be entered for the purpose of Appeal.

Respectfully submitted,



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